

# Nitrogen Balance in Postoperative Patients Receiving Parenteral Nutrition

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Fifteen patients were given parenteral nutrition with hyperosmolar glucose during the postoperative period (days 1 to 5): nine received an average of 10.5 gm of nitrogen and 2,340 kilocalories/day, six were given an average of 5.9 gm of nitrogen and 1,600 kilocalories/day. Eight patients (controls) received no nitrogen and 520 kilocalories/day. The results of this study confirm our early findings that total parenteral nutrition is capable of reversing the negative nitrogen balance of the immediate postoperative period; this reversal depends on administration of adequate nitrogen and calories. In patients with moderate surgical procedures, at least 8 gm of nitrogen and 1,800 kilocalories/day are required to correct the negative nitrogen balance. When total parenteral nutrition is instituted, adequate nitrogen and calories should be given, even if insulin is required to control hyperglycemia.

One of the major applications of total parenteral nutrition (TPN) has been in the management of the high-risk patients in the postoperative period. Previous studies have shown clearly that adequate nutritional management can minimize the catabolic response following surgery, and that the use of TPN can achieve positive nitrogen balance.<sup>1-3</sup>

In transferring the techniques of TPN from the specialized investigational inquiry to general clinical application, a number of practical problems have been encountered. The net effect of these problems is that the patient often receives considerably less nutritional support than would be considered optimal. The question is often raised: to what extent may one reduce the level of nutritional support below that which is considered ideal and still retain

the benefits of this form of therapy? To answer this question, a group of patients undergoing major abdominal surgical procedures and receiving TPN were selected for study. Metabolic balance studies were carried out during the early postoperative period. The nitrogen balance was used as a measure of the efficacy of TPN in minimizing the catabolic response to surgery.

## SUBJECTS AND METHODS

Twenty-three patients undergoing major abdominal surgical procedures were studied (Table 1). Eight received conventional intravenous therapy consisting of only the usual postoperative maintenance and fluid and electrolyte replacement, but no food was given by mouth; this group served as controls. The other 15 patients were given TPN; these patients were chosen for treatment with TPN by the attending surgeons in consultation with the parenteral nutrition team. The control group was selected by the investigators as having operative procedures comparable in magnitude to the patients receiving TPN. It should be emphasized that this was in no way a randomized selection process. The purpose was to study the effectiveness of TPN as applied in the general clinical setting, and the control group was selected to provide a standard for comparison.

All of the patients receiving TPN and four of the control patients were cared for at Vanderbilt University Hospital. The other four control patients were at the Nashville General Hospital.

Balance studies were carried out from the first through the fifth postoperative days. Parenteral intake of nitrogen, calories, sodium, potassium, and water, and oral intake of fluid were measured. Urinary output of nitrogen, sodium, and potassium were also determined. Fecal output was negligible in all patients during the study period, and was not included in the calculation of balances. Statistical analyses were performed according to standard methods. The Student-Fisher *t* test was used to estimate levels of significance.

All patients received a standard infusate for parenteral nutrition (Table 2). The amount given was determined in each case by the surgeons caring for the patient. Supplementation with con-

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Table 1.—Patients and Surgical Procedures

Nutrition Therapy	No./Patient Age, yr/Sex	Operation
Parenteral Nutrition	1/47/F	Resection of colostomy, anastomosis of colon
	2/62/M	Total gastrectomy, splenectomy, partial colectomy, construction of Hunt-Lawrence pouch
	3/52/F	Total gastrectomy, construction of Hunt-Lawrence pouch
	4/59/M	Vagotomy, conversion of gastroenterostomy to gastroduodenostomy, cholecystectomy
	5/47/F	Colon resection, colostomy
	6/74/F	Total gastrectomy, splenectomy, partial pancreatectomy, partial colectomy, construction of Hunt-Lawrence pouch
	7/73/F	Exploratory laparotomy, iliotransverse colostomy
	8/57/F	Massive small bowel resection
	9/57/F	Drainage of left subphrenic abscess
	10/75/M	Resection of duodenal stump with tube duodenostomy
	11/21/M	Resection of enterocutaneous fistula, small bowel resection
	12/52/F	Total colectomy
	13/56/M	Colon resection, anastomosis
	14/55/M	Closure of perforated ulcer, lysis of adhesions
	15/73/F	Cholecystectomy
Conventional Intravenous Therapy	16/18/M	Resection of marginal ulcer, vagotomy, hiatal hernia repair
	17/63/M	Endarterectomy of origin of lower pole renal artery
	18/69/M	Colon resection, anastomosis
	19/63/M	Vagotomy, pyloroplasty, repair of hiatal hernia, resection of esophageal diverticulum, gastrostomy
	20/69/M	Vagotomy, Pyloroplasty (died ten days postoperatively)
	21/63/F	Small bowel resection, oophorectomy
	22/59/F	Left aortofemoral bypass graft
	23/62/F	Colon resection, anastomosis

ventional intravenous fluids was given as necessary.

All procedures and techniques used for parenteral nutrition were as those previously described.<sup>8</sup> Nutrient solution for parenteral nutrition was prepared in the hospital pharmacy under rigid aseptic control. Precautions against sepsis during administration were followed routinely. Infusions were given into the superior vena cava through an indwelling catheter (silicone elastomer or polyethylene) via an external jugular or the subclavian vein. Meticulous care of the catheter entry site was emphasized.

## RESULTS AND COMMENT

All 15 patients receiving TPN were kept on therapy during the entire period without interruption. No deaths occurred during the study period, although one of the control patients (patient 20) died later during the postoperative period. No septic episode related to the catheter or to the infusate was observed. Figure 1 shows the caloric intake, nitrogen intake, nitrogen output, and nitrogen balance. It can be seen that the average daily nitrogen balance was +1.0 gm in patients receiving an average daily nitrogen intake of 10.5 gm and 2,340 kilocalories. The average daily nitrogen balance was -5.7 gm in patients receiving an average daily nitrogen intake of 5.9 gm and 1,590 kilocalories. In the patients receiving conventional intravenous therapy with no nitrogen intake and with only an average daily caloric intake of 520, an average daily nitrogen balance was -6.9 gm. It is also interesting to note in Fig 1 that the average daily loss from patients receiving parenteral nutrition with low intake of nitrogen and caloric was 11.6 gm; this is higher than that of patients receiving high nitrogen and caloric intake. Figure 2 shows that only one of the patients of the low nitrogen

and caloric intake group had a nitrogen balance of less than -2 gm; the daily caloric intake of this patient (patient 11) was 1,846. However, a negative nitrogen balance exceeding 2 gm/day was not observed in those receiving a nitrogen intake above 8 gm. Obviously, caloric intake is also an important factor that affects the nitrogen balance. It can be further noted in Fig 2 that a daily caloric intake of less than 1,800 kilocalories resulted in a more marked negative nitrogen balance; in general, nitrogen balance was positive or nearly maintained when an intake higher than 1,800 kilocalories and a nitrogen intake above 8 gm/day were given unless the surgical procedure was rather extensive. It should be pointed out also that one patient (patient 9) who received only 8.3 gm of nitrogen and 1,800 kilocalories/day had a positive nitrogen balance of 3.0 gm. This is probably due to the fact that this patient had a relatively moderate surgical procedure, drainage of left subphrenic abscess. It seems that the intake of 8 gm of nitrogen and 1,800 kilocalories is critical in minimizing the negative nitrogen balance.

Comparisons of nitrogen intake, nitrogen output, nitrogen balance, and caloric intake between patients receiving conventional intravenous therapy and those given parenteral nutrition are presented in Table 3. The average daily nitrogen balance for the high nitrogen and caloric intake groups was positive, and significantly different (0.5% level) from both the low nitrogen and caloric intake group and the control group. The nitrogen balance in the low nitrogen and caloric intake group was not substantially different from the control group. The urinary nitrogen loss in both high and low nitrogen and caloric intake groups receiving TPN was significantly higher (0.1%

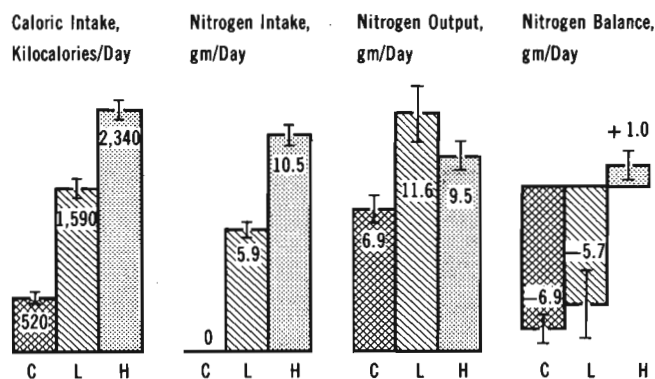


Fig 1.—Caloric intake, nitrogen intake, nitrogen output, and nitrogen balance of three groups of patients based on levels of caloric and nitrogen intake: C (cross hatching), control patients receiving conventional intravenous therapy; L (diagonal lines), patients receiving parenteral nutrition with low caloric and nitrogen intake; H (dots), patients receiving parenteral nutrition with high caloric and nitrogen intake. Numbers in columns are daily averages; vertical lines indicate standard errors of mean.

Table 2.—Composition of Solution for Parenteral Nutrition*	
Nutrient	Amount per Liter
Calories (as glucose)	900
Glucose	250 gm
Nitrogen†	4.17 gm
Electrolytes	
Sodium	23.6 mEq
Potassium	40 mEq
Magnesium	10 mEq
Chloride	27.5 mEq
Acetate	55.5 mEq
Calcium	5.5 mEq
Phosphorus	113 mg (elemental phosphorus)
Zinc sulfate	5 mg
Vitamins‡	
Ascorbic acid (C)	155 mg
Thiamine (B <sub>1</sub> )	5.5 mg
Riboflavin (B <sub>2</sub> )	1.1 mg
Pyridoxine (B <sub>6</sub> )	1.65 mg
Niacinamide	11 mg
Dexpanthenol	2.7 mg
Folic acid	100 µg
Vitamin B <sub>12</sub>	10 µg
Vitamin A	1,100 units
Vitamin D	110 units
Vitamin E	0.55 international units

\* Standard solution used for total parenteral nutrition at Vanderbilt University Hospital.

† As synthetic crystalline amino acid solutions: (1) 8% (Vein Amine) and (2) 8.5% (FreAmine).

‡ Given as 1.1 ml multiple vitamin injection, with supplemental ascorbic acid, folic acid, and vitamin B<sub>12</sub>.

Fig 2.—Relationship between nitrogen intake and nitrogen balance in patients receiving varying caloric intake.

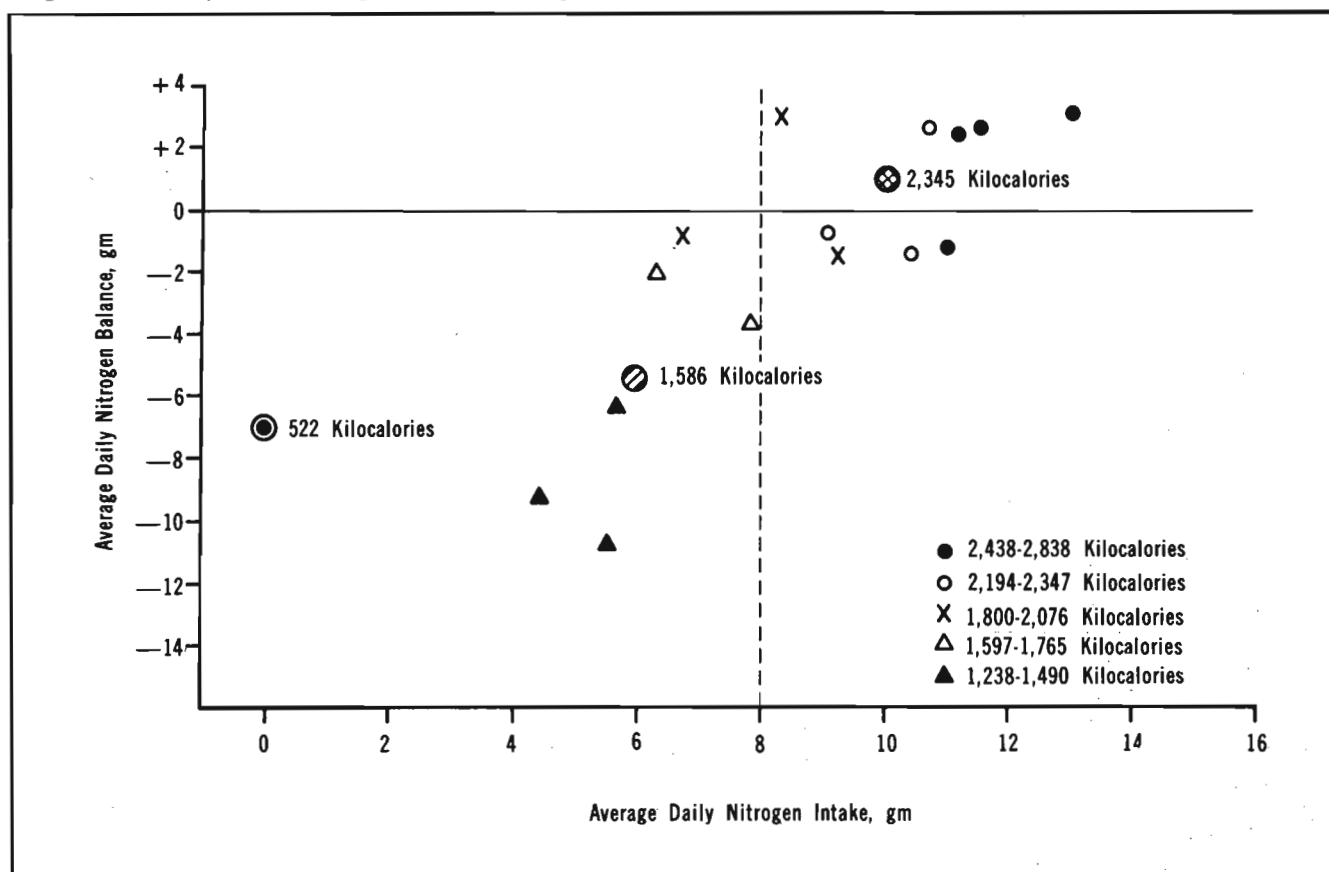


Table 3.—Comparison of Nitrogen Balance and Caloric Intake\*

Nutrition Therapy	Nitrogen Intake	Nitrogen Intake, gm/Day	Nitrogen Output, gm/Day	Nitrogen Balance, gm/Day	Caloric Intake, Kilocalories/Day
Parenteral Nutrition	High (9 patients)	10.50 ± 0.51	9.48 ± 0.71	±1.02 ± 0.70	2,345 ± 110
	Low (6 patients)	5.89 ± 0.28	11.55 ± 1.31	-5.66 ± 1.68	1,586 ± 95
Conventional Intravenous Therapy	Control (8 patients)	0	6.88 ± 0.71	-6.88 ± 0.71	522 ± 33 (5 patients)

\* Values expressed as daily averages ± SE. Tests for significance (Student-Fisher t test): nitrogen intake, high vs low: 0.1% level; nitrogen output, high vs low: 10% level; nitrogen output, high or low vs control: 1% level; nitrogen balance, high vs low: 0.5% level; nitrogen balance, high vs control: 0.1% level; nitrogen balance, low vs control: NS.

Table 4.—Average Daily Sodium and Potassium Balance

Parenteral Nutrition	Patient No.	Sodium, mEq			Potassium, mEq		
		Intake	Output	Balance	Intake	Output	Balance
High Nitrogen	1	113	120	-7	126	80	+46
	2	71	70.8	+0.2	111	51	+60
	3	99	94.8	+4.2	108	52	+56
	4	74	72	+2	107	115	-8
	5	114	97	+17	105	56	+49
	6	102	103	-1	103	95	+8
	7	140	129	+11	88	97	-9
	8*	...	...	...	...	...	...
	9	106	112	-6	89	59	+30
	Mean	102	100	+2	105	76	+39
Low Nitrogen	10*	...	...	...	...	...	...
	11	109	50	+59	65	82	-17
	12	95	126	-31	62	74	-12
	13	61	108	-47	54	54	0
	14*	...	...	...	...	...	...
	15	81	69	+12	43	82	-39
	Mean	86	88	-2	56	73	-17

\* Urine not available for sodium and potassium measurement.

level) than that of the controls. The patients receiving parenteral nutrition with low nitrogen and caloric intake had a somewhat greater nitrogen loss than those with a high intake, however, this is not statistically significant (10% level). The high nitrogen loss is probably, at least in part, due to the low caloric intake; and the amino acids given were metabolized to meet the energy need.

Sodium and potassium balances in patients receiving parenteral nutrition with a high and low intake of nitrogen are presented in Table 4. The average daily sodium balance was nearly 0 for both groups. The results suggest that the need for sodium may be about 100 mEq/day in patients receiving parenteral nutrition, provided that the patient has a normal renal function and has no excessive loss. The potassium balance was positive in the patients with high intake of nitrogen and calories and negative in those with low intake of nitrogen and calories, although potassium losses were about the same. Undoubtedly, the negative potassium balance was due, in part, to the loss of intracellular potassium and/or inadequate caloric and nitrogen intake to promote potassium utilization.

Although the administration of an average of 10.5 gm of nitrogen and 2,340 kilocalories daily resulted in an average daily positive nitrogen balance in the early postoperative period in patients studied, some patients in this group had a slight negative nitrogen balance. The magnitude of negative nitrogen balance in patients given about 6.0 gm of nitrogen and 1,600 kilocalories/day was not substantially different from that in those receiving conventional intravenous therapy. The reason for this is unknown. One might suggest that the administered amino acids in patients receiving low nitrogen and low caloric intake were metabolized for energy. This would account for the failure of TPN to reduce the magnitude of postoperative nitrogen loss. Elman showed that amino acids given in the absence of glucose had little effect in promoting positive nitrogen balance, and that it was necessary to infuse the two simultaneously.<sup>9</sup> Similar results were reported by McNair et al.<sup>10</sup>

The study of Rush et al.<sup>11</sup> showed that positive nitrogen balance during the postoperative period could be achieved with a high level of amino acid and glucose intake. In 19

patients, a level of nitrogen intake of 0.21 to 0.34 gm/kg/day was used. This was somewhat higher than the high nitrogen intake group in the present study. Caloric intake of the two studies was comparable.

Lawson<sup>3</sup> studied nitrogen balance in four patients with daily intakes of 2,600 to 3,200 kilocalories and 6 to 12 gm of nitrogen. In these patients, the nitrogen balance was rendered less negative, but positive balance was not achieved. These patients were not strictly comparable to the present study because they were not immediately postoperative and they were subjected to more severe stress.

The evidence presented in the present study suggests that in patients with postoperative stress of moderate severity, at least 8 gm of nitrogen and 1,800 kilocalories/day are required to have a substantial favorable effect on the nitrogen balance. However, it appears likely that a daily intake of 12 to 13 gm of nitrogen and 2,500 kilocalories should be given to achieve positive nitrogen balance in most of the postoperative patients. It may be pointed out that nitrogen and calorie requirements depend on the conditions of patients. Increase in the severity of stress and the presence of sepsis would increase the need for additional nitrogen and calories. The present work does not provide any information as to which of the two factors—nitrogen or calories—is more important in promoting positive nitrogen balance. Further study is necessary.

It is important to note that one third of the patients in the study were given less than 8 gm of nitrogen and 1,800 kilocalories by the surgeons caring for them. This level of intake corresponds to less than 2 bottles or 2 liters of the parenteral nutrition solution, which furnishes 8.33 gm of nitrogen and 1,800 kilocalories. In starting a patient on TPN therapy, few complications occur at low levels of administration. Above 2 bottles or 2 liters of the solution per day, which furnishes 500 gm of glucose, hyperglycemia and glycosuria often occur, especially in patients with severe stress, and insulin administration may be necessary. The volume of fluid required may be excessive, especially considering that many postoperative patients require 1 to 2 liters per day of fluids other than that for parenteral nutrition. These factors contribute to a general reluctance on the part of the surgeon caring for the patient to use TPN aggressively. Because of this, many patients are never given more than 2 liters per day.

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## Nonproprietary Name and Trademarks of Drug

Dexpanthenol—Alcopan-250, Ilopan, Motilyn.

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## Editorial Comment

The message in this study is for anyone who might have thought that a little parenteral nutrition, like "a little wine for thy stomach's sake," is a good thing. Parenteral nutrition, in order to be effective, must provide completely for the patient's increased metabolic need for calories after an operation and must provide sufficient nitrogen to allow positive balance. Providing some nitrogen with inadequate calories has again been found to increase nitrogen in the urine but not to reduce the negative nitrogen balance. It would have been interesting to have included another group of patients in this study who would receive only amino acids and no glucose. This would have determined if nitrogen balance approaches 0 due to increased utilization of body fats and decreased protein breakdown, as suggested by Blackburn et al (*Am J Surg* 125:447, 1973). As to the relative importance of calories and nitrogen, positive nitrogen balance is impossible without nitrogen being given, and anabolism is impossible without adequate calories.

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